Treatment For The Large Aggressive Benign Lesions Of The Jaws

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Abstract

Objectives Our aim was to evaluate the clinical outcome of the conservative management of the significantly large benign aggressive lesions of the jaws.

Subjects and Methods Twenty-two patients were reviewed regarding the demographic, radiographic, and operative findings. Patients were treated by decompression followed by curettage or only with curettage.

Results No bone grafts were used. Mean follow-up time was 56.2 months. The mandible was more affected than the maxilla. Two of the ameloblastoma, two of the keratocystic odontogenic tumours, and one odontogenic myxoma were recurred.

Conclusions Despite the low number of the patients, it is concluded that the conservative management is predictable for the management of the benign aggressive lesions in order to reduce morbidity instead of directly performing radical surgery. The life during follow-up is mandatory in the situation of performing conservative surgery for the management of large aggressive lesions with high recurrence rate.

Keywords Keratocyst · Ameloblastoma · Recurrence · Management

Introduction

The present study reviewed the large (larger than 50 mm) benign aggressive lesions with high recurrence rate including KCOT, ameloblastoma, central giant cell

granuloma, odontogenic myxoma, aneurysmal bone cyst, arterio-venous malformation, desmoplastic fibroma, and calcifying epithelial odontogenic tumour (Pindborg tumour), which were treated conservatively, during the last 9 years. In the present study, the majority of the samples were ameloblastoma and KCOT.

According to the 2005 World Health Organisation (WHO) classification, the most frequent odontogenic tumours follow the sequence: KCOT, ameloblastoma, and odontomas [1]. Many treatment techniques for ameloblastomas have been suggested, which include decompression, enucleation, marginal resection, and aggressive resection as partial or total resection [2].

The surgical treatment options of KCOT range from conservative marsupialization and enucleation, with and without the use of adjunctive treatments, to more aggressive en bloc resection. The reported recurrence rate of KCOT is relatively high, with a range of 5–70% depending on the method of treatment [3].

Conservative and radical surgeries have been used for the management of these lesions by various investigators. Aggressive approaches may lead to deformities. Resection without reconstruction may create severe post-operative deformities that have adverse psychosocial consequences, particularly in young patients; while resection with reconstruction may prevent such adverse psychosocial consequences, it entails additional surgery and is prohibitively expensive [4].

In the literature, limited data are present which evaluate the conservative management of the large (longer than 50 mm) benign aggressive lesion. The majority of the papers are case series [3, 5–8].

The present study, differently than the previously published studies, aimed to evaluate retrospectively the long-term results of the conservative management for

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specifically large benign aggressive lesions. The risk of the recurrences associated with the lesions, intraoperative and post-operative complications were also presented.

Patients and Methods

To address the research purpose, we designed and implemented a retrospective cohort study. The study population was composed of the patients presenting to the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Istanbul University for evaluation and management of the benign lesions of the jaw between January 2006 and January 2015. This retrospective study was reviewed and approved by the Institutional Review Board of the Faculty of Dentistry, Istanbul University. The recommendations of the Helsinki declaration were thoroughly maintained during this study.

To be included in the study sample, patients had to (1) have lesions primarily occurring in the maxilla or mandible; (2) have a histopathological report demonstrating the final diagnosis of any benign aggressive lesion of the jaws according to the 2005 WHO odontogenic and non-odontogenic tumour classification [1]; (3) have lesion more than 50 mm of diameter, and (4) have treated with conservative surgery.

Patients who were diagnosed with nevoid basal cell carcinoma syndrome, were diagnosed with benign lesions of the jaws with lower recurrence rate (odontoma, radicular cyst, dentigerous cyst, orthokeratotic odontogenic cyst, etc.), were treated before in another department, were treated by radical surgery, or had follow-up less than 2 years were excluded from the study.

The predictor variable for this study was conservative treatment. Other study variables were grouped into demographic, medical, radiographic, and operative categories. Demographic and medical variables included age and gender. The radiographic variables were location of the lesion (maxilla or mandible, anterior, or posterior), association with impacted teeth, radiographic size of the lesion, and locularity (unilocular or multilocular radiographic appearance). The radiographic size of each lesion was recorded as the largest diameter of the lesion in any dimension estimated using panoramic radiographs taken before treatment.

The primary outcome variable of the study was cure or recurrence. The authors investigated how the conservative surgery affects the recurrence rate for the treatment of the large lesions. The time to cure or recurrence had been verified retrospectively.

Statistical Analysis

Statistical calculations were performed with NCSS 2007 programme for Windows. Descriptive statistics and the comparison of the recurrent and non-recurrent groups were evaluated by Chi-square and independent *t* test. Potential significant predictors and prognostic variables were considered factors for the outcome of time to recurrence based on univariate Cox regression analyses. The biologic variables of age and gender, the operative variable, and nearly statistically significant variables ($p \leq 0.15$) as locularity and size, identified using univariate Cox regression analyses, were used to build the multivariate Cox proportional hazards regression model to identify variables associated with time to disease recurrence. In the multivariate model, statistically significant variables were set at $p \leq 0.05$.

Statistical and survival methodologies were based on Kaplan–Meier analysis, and Cox proportional hazards models were used to assess recurrence risks and time-to-recurrence survival analysis [9].

Results

In the present cohort, 22 lesions in 22 patients treated with decompression followed curettage or only with curettage. Demographic findings are summarized in Table 1. The mean age was 38.0 years. Thirteen patients (59.09%) were male, and 9 (40.90%) were female. During the study interval, 8 KCOT, 4 ameloblastoma, 4 odontogenic myxoma, 1 aneurysmal bone cyst, 2 central giant cell granuloma, 1 arterio-venous malformation, 1 desmoplastic fibroma, and 1 Pindborg tumour were evaluated and treated at the study institution. Twenty (90.9%) lesions were located in the posterior mandible, and 2 (9.09%) lesions were located at the anterior of the mandible. Four (18.80%) were associated with impacted teeth, and only 2 (9.09%) lesions were located in the maxilla. The largest diameter of the lesions studied was found as 84 mm. The average diameter was 61.59 mm, 13 lesions (59.09%) were unilocular, and 9 (40.90%) were multilocular (Figs. 1, 2). Three (13.63%) patients were treated with decompression followed by curettage, and 19 (86.36%) patients were treated with only curettage. The overall mean follow-up time was 56.27 ± 25.56 months (median 60 months; interquartile range 24–72 months). The time interval between operation and recurrence varied from 18 to 66 months. Most recurring lesions, however, presented within 3 years of operation. Decompression treatment duration varied 6–8 months (Figs. 3, 4). In this cohort, 5 (22.7%) patients developed recurrences. These included two patients with ameloblastoma, two patients with KCOT,

Table 1 Descriptive statistics

Age	38.05 ± 17.72	
Gender		
Male	13	59.09%
Female	9	40.91%
Location		
Mandible	20	90.91%
Maxilla	2	9.09%
Location 1		
Posterior	20	90.91%
Anterior	2	9.09%
Locularity		
Unilocular	13	59.09%
Multilocular	9	40.91%
Associated with impacted teeth		
No	18	81.82%
Yes	4	18.18%
Surgical method		
Curettage	20	90.91%
Decompression and curettage	2	9.09%
Time to recurrence (mean)	45.73 ± 23.99	
(Median)	42 (24–61.5)	
Duration of follow-up T (mean)	56.27 ± 25.56	
(Median)	60 (24–72)	
Size (mm)	61.14 ± 10.45

Fig. 1 Multilocular view of the ameloblastoma of the mandible

and one patient with odontogenic myxoma. One of the patients with the ameloblastoma of the mandible had a second recurrence. Therefore, he had undergone radical excision and placement of a reconstruction plate was performed. Description of the recurrent and non-recurrent lesions according to the age, gender, location, and association with the impacted teeth and surgical method is summarized in Table 2. The presence of the multilocularity in recurrent lesions (80%) was statistically higher than its presence in the non-recurrent lesions (29.41%, $p = 0.043$) (Table 2). No statistically significant variable for the

Fig. 2 Unilocular view of the desmoplastic fibroma of the mandible **Fig. 3** Pre-operative view of a KCOT of the mandible **Fig. 4** View of the reduced lesion 8 months after decompression

presence of the recurrence has been found in univariate and multivariate Cox proportional hazards models (Tables 3, 4).

Intraoperative bleeding was significantly observed only with the two patients diagnosed with aneurysmal bone cyst and central giant cell granuloma of the posterior mandible (Fig. 5). On the other hand, the young girl with an arterio-venous malformation did not show any intraoperative bleeding because of the pre-operative selective embolization procedure. One patient with KCOT of the mandible

Table 2 Description of the recurrent and non-recurrent lesions

	Recurrence (–) <i>n</i> : 17		Recurrence (+) <i>n</i> : 5		<i>p</i>
Age	37.88 ± 19.33		38.6 ± 12.8		0.939
Gender					
Male	9	52.94%	4	80.00%	0.279
Female	8	47.06%	1	20.00%	
Location A					
Mandible	15	88.24%	5	100.00%	0.421
Maxilla	2	11.76%	0	0.00%	
Location B					
Posterior	16	94.12%	4	80.00%	0.334
Anterior	1	5.88%	1	20.00%	
Locularity					
Unilocular	12	70.59%	1	20.00%	0.043
Multilocular	5	29.41%	4	80.00%	
Associated with impacted teeth					
No	14	82.35%	4	80.00%	0.905
Yes	3	17.65%	1	20.00%	
Surgical method					
Curettage	16	94.12%	4	80.00%	0.334
Decompression and curettage	1	5.88%	1	20.00%	
Follow-up (month)	50.47 ± 23.34		29.6 ± 20.55		0.048
Size (mm)	59.59 ± 10.39		66.4 ± 9.86		0.208

Table 3 Univariate Cox proportional hazards analyses: factors associated with time to recurrence

	Hazard ratio	95% CI		<i>p</i>
Age	1.01	0.95	1.06	0.859
Gender	2.21	0.23	21.29	0.492
Location (mandible–maxilla)	24.91	0.00	102.80	0.609
Location (posterior–anterior)	0.24	0.03	2.37	0.224
Locularity	0.13	0.01	1.21	0.073
Associated with impacted teeth	0.80	0.09	7.31	0.842
Surgical method	0.57	0.06	5.18	0.613
Size (mm)	1.07	0.98	1.16	0.131

CI confidence interval

Table 4 Multivariate Cox regression analysis: factors associated with time to recurrence

	Hazard ratio	95% CI		<i>p</i>
Age	0.94	0.83	1.07	0.341
Gender	9.35	0.18	479.10	0.266
Locularity	0.06	0.00	2.71	0.144
Size (mm)	1.01	0.90	1.14	0.834

CI confidence interval

developed secondary infection. One patient with an aggressive odontogenic myxoma (Fig. 6) received reconstruction plate during the operation at the anterior part of

Fig. 5 Aggressive odontogenic myxoma of the mandible

the mandible in order to prevent a possible fracture. No post-operative fracture of the mandible was observed despite the conservative treatment of the large lesions

Fig. 6 Axial view of a central giant cell granuloma

during the 9 years of follow-up. On the other hand, the dislodgement of the decompression tube was observed in two patients. One patient had extraoral fistulae at the mandible, showing the recurrence of a KCOT. No bone grafts were used in any case during the operation. Table 5 presents the Kaplan–Meier survival estimates. Based on Kaplan–Meier analyses, the 6-year estimate of disease-free lesions was 64.2%.

Discussion

The present study evaluated the outcome of the conservative management of the large benign aggressive lesions of the jaws. A slight male predominance was observed (13/9). The age of the patients ranged from 14 to 81 years. Most of the cases were distributed with a peak incidence in the third decade. The majority of the lesions (90.9%) were located at the posterior side of the mandible.

The literature still shows some debate regarding the most appropriate method for management of the benign aggressive lesions of the jaws. Radical resection provides

efficient removal of the affected bone and soft tissue in continuity with the tumour, which decreases the risk of recurrence. However, resection of the inferior alveolar nerve and extraction of the teeth will lead to poorer oral function and causes permanent anaesthesia of the lower lip. On the other hand, possible disadvantages using conservative approach, as decompression technique, are that it usually requires two surgical procedures, and the time necessary for the treatment is comparatively long [2, 10–12].

It is evident that decompression of odontogenic cyst-like lesions does decrease the average lesion size anywhere from 50 to 81% over a range of decompression times from 7 to 44 months [2, 13]. In the present study, two patients received decompression. One of them was a male with a large KCOT of the mandible. After 8 months of decompression, the volume of the cyst reduced more than 60%. On the other hand, the second patient with a KCOT of the total ramus showed recurrence despite the management of the decompression. The recurrence was associated with the difficult access of the tumour which including also the condyle of the mandible.

Some of the investigators used Carnoy solution for the management of KCOT in order to prevent recurrence. Prospective randomized studies are needed on this topic [14]. Additionally, the solution had become virtually unobtainable in California, as the California Occupational Health and Safety Administration had classified the chloroform in it as a carcinogen [11]. The authors of the present study performed routinely removal of the teeth associated with the pathological lesions and use a surgical large tungsten-carbide burr to remove the remained cortical bone after curettage, in order to prevent a possible recurrence without using Carnoy solution. This technique is similar reported by Pogrel [11]. Differently than our technique he reported that he preferred to use methylene blue for determining the bony margins in order to remove it with a pineapple-type bur.

In the present study, the time interval between operation and recurrence varied from 18 to 66 months. Many reports have revealed a recurrence range of 1–15 years, with 2–5 years being the most common time as reported in our study. In this study, two ameloblastomas of the mandible were recurred 18 and 21 months after curettage, respectively [15].

Recurrence of KCOT occurs for several reasons. Incomplete removal of the cystic lesion allows new cyst formation or epithelial islands in the wall of the original cyst remain in the surrounding bone or soft tissue [7]. New KCOTs can also develop from the basal layer of the oral epithelium. Size, location, and inadequate surgical treatment of the KCOT also contribute to possible recurrence [16]. The propensity for KCOT to recur is more during the

Table 5 The 6-year estimate of disease-free lesions based on Kaplan–Meier analyses

	At risk (n)	Recurrence	Disease-free (%)
0 month	22	0	100
12 months	22	0	100
24 months	14	1	90.4
36 months	14	0	86.8
48 months	6	0	86.8
60 months	6	2	80.2
72 months	4	1	64.2
Medians for survival time			76.31 ± 7.55 (61.5–91.11)

first 5 years. Patients with a KCOT require lifelong after-care because relapses of KCOTs can arise even after 10 or more years [12]. In our study, one of the KCOT of the ramus recurred 25 months after curettage and the second one recurred 66 months after operation. Another recurrent lesion of this study was a very aggressive odontogenic myxoma of the anterior mandible. The lesion was recurred 18 months after curettage consisting with the current literature. An aggressive curettage was performed again, but the recurrent lesion was quite small. Only three cases of odontogenic myxoma with unusual calcifications were reported in the literature [17]. In our case also calcifications were noted.

The authors' opinion was to wait for the physiological bone regeneration after the operations of these large benign lesions presented. No bone graft material was used intra-operatively in order to prevent a possible infection. The majority of the patients included in this study received also dental implants which were placed in the spontaneously healed bone defects after the curettage. These findings suggest that even large defects may heal without using any graft materials when the surgeon carefully preserves the periosteum and bone walls as the sources for osteogenesis, even if they are very thin. The surgical approach through the bone to cysts or other benign pathological changes must be as low vestibular as is possible, to preserve the bone borders of the alveolar part of the mandible. The surgical approach through the alveolar crest impairs the height of the mandible and does not allow good prosthodontic rehabilitation [18, 19].

The weaknesses of the present study included the retrospective case series design and small numbers of patients. However, the inclusion criteria of this study are specific because of the large size (more than 50 mm), the clinical behaviour (benign aggressive) of the lesions and also because of the long time of follow-up. Five patients (22.7%) had a recurrent lesion with a mean time to recurrence of 45.7 months. The Kaplan–Meier 6-year estimate for disease recurrence was found as 64.2%. Another important finding was that the recurrent lesions showed statistically significant multilocularity than non-recurrent lesions ($p = 0.043$). This finding has been reported in current literature [9]. On the other hand, no statistically significant variable for the presence of the recurrence has been found in univariate and multivariate Cox proportional hazards models.

Another limitation is that we had no control group for the lesions treated by aggressive surgery. On the other hand, there are no large case series documenting the conservative treatment outcomes for these large benign aggressive lesions in long term; therefore, our study can inform the practitioners who may hesitate to perform

aggressive or conservative surgery for the patients with the large and aggressive benign lesions of the jaws.

Conclusions

The authors of the present study suggest to perform conservative surgery as an initial approach instead of performing directly aggressive surgery. This approach reduces the morbidity of the aggressive surgeries and preserves the anatomical structures. On the other hand, life during follow-up is mandatory in order to early diagnose of a possible recurrence. Early diagnosis of a small recurrent lesion may be treated again with the conservative approach. The aggressive treatment may be performed in the situation of unsuccessful conservative surgeries.

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Compliance with ethical standards

Conflict of interest None.

References

1. Servato JP, Prieto-Oliveira P, de Faria PR, Loyola AM, Cardoso SV (2013) Odontogenic tumours: 240 cases diagnosed over 31 years at a Brazilian university and a review of international literature. *Int J Oral Maxillofac Surg* 42:288–293
2. Xavier SP, de Mello-Filho FV, Rodrigues WC, Sonoda CK, de Melo WM (2014) Conservative approach: using decompression procedure for management of a large unicystic ameloblastoma of the mandible. *J Craniofac Surg* 25:1012–1014
3. Zhou H, Hou R, Ma Q, Wu K, Ding Y, Qin R et al (2012) Secondary healing after removal of large keratocystic odontogenic tumor in the mandible: enucleation followed by open packing of iodoform gauze. *J Oral Maxillofac Surg* 70:1523–1530
4. Kumar V (2015) Conservative surgical approach to aggressive benign odontogenic neoplasm: a report of three cases. *J Korean Assoc Oral Maxillofac Surg* 41:37–42
5. Caixeta Guimarães A, de Cassia Dutra, Ferreira Santos M, Machado de Carvalho G, Takahiro Chone C, Nizam Pfeilsticker L (2013) Giant keratocystic odontogenic tumor: three cases and literature review. *Iran J Otorhinolaryngol* 25:245–252
6. Pogrel MA, Jordan RCK (2004) Marsupialization as a definitive treatment for the odontogenic keratocyst. *J Oral Maxillofac Surg* 62:651–655
7. de Molon RS, Verzola MH, Pires LC, Mascarenhas VI, da Silva RB, Cirelli JA et al (2015) Five years follow-up of a keratocyst odontogenic tumor treated by marsupialization and enucleation: a case report and literature review. *Contemp Clin Dent* 6(Suppl 1):S106–S110
8. Liang YJ, He WJ, Zheng PB, Liao GQ (2015) Inferior alveolar nerve function recovers after decompression of large mandibular cystic lesions. *Oral Dis* 21:674–678
9. Kinard BE, Chuang SK, August M, Dodson TB (2013) How well do we manage the odontogenic keratocyst? *J Oral Maxillofac Surg* 71:1353–1358

10. Dandriyal R, Gupta A, Pant S, Baweja HH (2011) Surgical management of ameloblastoma: conservative or radical approach. *Natl J Maxillofac Surg* 2:22–27
11. Pogrel MA (2015) The keratocystic odontogenic tumour (KCOT)—an odyssey. *Int J Oral Maxillofac Surg* 44:1565–1568
12. Ebenezer V, Ramalingam B (2014) Importance of different modalities of treatment for the management of keratocystic odontogenic tumour with five year follow-up. *J Clin Diagn Res* 8:225–228
13. Schlieve T, Miloro M, Kolokythas A (2014) Does decompression of odontogenic cysts and cystlike lesions change the histologic diagnosis? *J Oral Maxillofac Surg* 72:1094–1105
14. Zecha JA, Mendes RA, Lindeboom VB, van der Waal I (2010) Recurrence rate of keratocystic odontogenic tumor after conservative surgical treatment without adjunctive therapies—a 35-year single institution experience. *Oral Oncol* 46:740–742
15. Bansal S, Desai RS, Shirsat P, Prasad P, Karjodkar F, Andrade N (2015) The occurrence and pattern of ameloblastoma in children and adolescents: an Indian institutional study of 41 years and review of the literature. *Int J Oral Maxillofac Surg* 44:725–731
16. Johnson NR, Batstone MD, Savage NW (2013) Management and recurrence of keratocystic odontogenic tumor: a systematic review. *Oral Surg Oral Med Oral Pathol Oral Radiol* 116:e271–e276
17. Lahey E, Woo SB, Park HK (2013) Odontogenic myxoma with diffuse calcifications: a case report and review of the literature. *Head Neck Pathol* 7:97–102
18. Chiapasco M, Rossi A, Motta JJ, Crescentini M (2000) Spontaneous bone regeneration after enucleation of large mandibular cysts: a radiographic computed analysis of 27 consecutive cases. *J Oral Maxillofac Surg* 58:942–948
19. Ihan Hren N, Miljavec M (2008) Spontaneous bone healing of the large bone defects in the mandible. *Int J Oral Maxillofac Surg* 37:1111–1116